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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/709,739	05/26/2004	Itzhak Bentwich	050992.0302.00USCP	3738
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ROSETTA-GENOMICS c/o PSWS 700 W. 47TH STREET SUITE 1000 KANSAS CITY, MO 64112			EXAMINER SCHNIZER, RICHARD A	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 09/26/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/709,739

**Applicant(s)**

BENTWICH ET AL.

**Examiner**

Richard Schnizer, Ph. D.

**Art Unit**

1635

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 26, 31, 33 and 35-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 26, 31, 33 and 35-37 is/are rejected.
- 7) ☒ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 May 2004 and 02 January 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

An amendment after final was received and entered on 8/5/02.

Claims 26, 31, 33, and 35-37 remain pending and under consideration.

Finality of the previous action is hereby withdrawn in favor of this new NON-FINAL action.

The previous rejections under 35 USC 102 and 103 citing Pfeffer et al (US 20050222067) are withdrawn because the Office has found, and Applicant has shown in the amendment filed 8/5/02, that the priority document PCT/IL03/00998 discloses instant SEQ ID NOS: 4204050 and 117937. Accordingly the instant claims are entitled to a filing date of 11/23/03, and Pfeffer is not available as prior art.

### ***Specification***

The specification is objected to because it refers to Tables 1-14 at paragraph 27 at pages 21 and 22, and elsewhere e.g. paragraphs 211-214 at pages 92 and 93, and paragraphs 504-506 on pages 204-206, but the specification as filed does not contain any Tables labeled 1-14. The specification as filed appears to contain tables that may correspond to Tables 12-14 (indexed as a 69 page document labeled "Specification", viewable on public PAIR), but these are not labeled as Tables anywhere in the document. It is noted that the specification indicates that Tables 1-14 were supplied on CDs and are incorporated by reference (paragraph 27 at pages 21 and 22). However, such incorporation by reference appears to be improper, as discussed more fully under 35 USC 112, first paragraph rejections below.

### ***Claim Objections***

Claims 31, 33, 36, and 37 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 31 is drawn to a vector comprising a nucleic acid of claim 26. However, claim 26 is drawn to an isolated nucleic acid consisting of a nucleic acid sequence. The claim uses closed language to describe the nucleic acid. As a result, claim 31 does not further limit the isolated nucleic acid set forth in claim 26, instead, it improperly adds matter which is not accounted for in claim 26, i.e. a vector. Because it does not further limit claim 26, but instead broadens it, it is an improper dependent claim. Claim 36 is objected to for the same reason. Similarly, claims 33 and 37 are objected to for similar reasons. To the extent that the recited probes **consist** of SEQ ID NOS: 4204050 or 117937, they do not further limit claims 26 or 35. Also, to the extent that they may **comprise** components not present in SEQ ID NOS: 4204050 or 117937, such as labels or further sequences, they improperly add matter which is not accounted for in claim 26 or claim 35.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26, 31, 33, and 35-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 26 is drawn to a) an isolated nucleic acid consisting of SEQ IS NO: 4204050, b) an RNA equivalent thereof, or the complement a) or b). Claim 31 is drawn to a vector comprising the nucleic acid of claim 26, and claim 33 is drawn to a probe comprising the nucleic acid of claim 26.

Claim 35 is drawn to a) an isolated nucleic acid consisting of SEQ IS NO: 117937, b) an RNA equivalent thereof, or the complement a) or b). Claim 36 is drawn to a vector comprising the nucleic acid of claim 35, and claim 37 is drawn to a probe comprising the nucleic acid of claim 35.

A search of the art indicates that claimed SEQ ID NOS: 4204050 and 117937 correspond to fragments of a cytomegalovirus genome (see Pfeffer et al, (US 20050222067, of record)). The specification makes reference to genome address messenger (GAM) oligonucleotides and genome record (GR) polynucleotides throughout the disclosure. It appears that SEQ ID NOS: 4204050 and 117937 are considered to be GAM oligonucleotides which are miRNA-like molecules that can suppress the expression of a target mRNA. See e.g. the instant specification at paragraph 198 at page 198, and paragraph 205 bridging pages 90 and 91.

The specification at paragraph 213 on page 93 indicates that the

specific functions and accordingly the utilities of each of a plurality of GAM oligonucleotides that are described by Fig. 1 are correlated with and may be deduced from the identity of the GAM TARGET GENES inhibited thereby, and whose functions are set forth in Table 8, hereby incorporated herein.

Studies documenting the well known correlations between each of a plurality of GAM TARGET GENES that are described by Fig. 1 and the known gene functions and related diseases are listed in Table 9, hereby incorporated herein.

Accordingly Tables 8 and 9 contain material that is essential to determining the utility and enablement of the claimed invention. However, it appears that Tables 8 and 9 were not intended to be part of the specification as filed. These Tables were supplied on compact discs, and the were incorporated by reference at paragraph 27 at page 21 of the specification as filed. This appears to be an improper incorporation by reference. MPEP 608.01(p) indicates that in any application that is to issue as a U.S. patent, essential material may only be incorporated by reference to a U.S. patent or patent application publication. The Tables in question, and the essential information therein, are not a U.S. patent or a patent application publication. Note also that MPEP 608.01 (p) indicates that when incorporating material by reference "[p]articular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found." No specific reference is made to any part of Table 8 or 9 pertaining to the claimed SEQ ID NOS. The Examiner has attempted to view the Tables on the supplied CDs, but the files are too large to open using the available software.

Because the specification as filed improperly incorporates by reference subject matter that is essential to the use of the claimed invention, the specification fails to

provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, as required by the first paragraph of 35 U.S.C. 112.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Ghazal et al (WO/200257437).

Ghazal taught a yeast artificial chromosome vector comprising nucleotides 163187-163253, which are identical to instant SEQ ID NO: 4204050, and which comprise instant SEQ ID NO: 117937. Accordingly Ghazal taught a vector that comprised a sequence consisting of instant SEQ ID NO: 4204050, and a sequence consisting of instant SEQ ID NO: 117937. See abstract and alignment below.

```
Qy          1  GACAGCCTCCGGATCACATGGTTACTCAGCGTCTGCCAGCCTAAGTGACGGTGAGATCCA 60
              |||
Db    163187  GACAGCCTCCGGATCACATGGTTACTCAGCGTCTGCCAGCCTAAGTGACGGTGAGATCCA 163246

Qy          61  GGCTGTC 67
              |||
Db    163247  GGCTGTC 163253
```

'Qy' refers to instant SEQ ID NO: 4204050, and 'Db' refers to the sequence of Ghazal.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 35 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ghazal et al (WO/200257437) in view of Buck et al (BioTechniques 27: 528-536, 1999).

Ghazal taught a yeast artificial chromosome vector comprising at least a portion of a human cytomegalovirus genome, wherein the portion includes nucleotides 163187-163253, which are identical to instant SEQ ID NO: 4204050, and which comprise instant SEQ ID NO: 117937. Accordingly Ghazal taught a vector that comprised a sequence consisting of instant SEQ ID NO: 4204050, and that comprised a sequence consisting of instant SEQ ID NO: 117937.

Ghazal did not teach an isolated nucleic acid consisting of SEQ ID NO: 117937, or a probe comprising SEQ ID NO: 117937. However, it is clear that it was obvious to those of ordinary skill in the art that sequencing primers were required in order to obtain the sequence disclosed in Ghazal. It is considered obvious for the reasons set forth



below to make primers of the same length of SEQ ID NO: 117937, and further, these primers can be considered to be probes.

Buck analyzed the effect of primer design strategy on the performance of DNA sequencing primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that every single primer worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, every single control primer functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

It would have been obvious to one of ordinary skill in the art at the time of the invention to synthesize instant SEQ ID NO: 117937 as a primer in the process of determining the sequence disclosed in Ghazal. In view of the teachings of Buck,

sequencing primers can be synthesized essentially anywhere along a given sequence of interest, and under optimal conditions they will reasonably be expected to perform adequately to yield sequence data. See page 533, left column, first full paragraph, and paragraph bridging pages 535 and 536. It would have been obvious to select a primer length of 22 nucleotides because those of ordinary skill normally use sequencing primers of 19-24 nucleotides in length (see Buck abstract.). Accordingly, any 22 nucleotide fragment represented in either strand of the vector of Ghazal is considered to be obvious.

Claims 26 and 33, and are rejected under 35 U.S.C. 103(a) as being unpatentable over Ghazal et al (WO/200257437) in view of Hogan (US Pat. 5,541,308, July 30, 1996).

Ghazal taught a yeast artificial chromosome vector comprising at least a portion of a human cytomegalovirus genome, wherein the portion includes nucleotides 163187-163253, which are identical to instant SEQ ID NO: 4204050. Accordingly Ghazal taught a vector that comprised a sequence consisting of instant SEQ ID NO: 4204050.

Ghazal did not teach an isolated nucleic acid consisting of SEQ ID NO: 4204050, or a probe comprising SEQ ID NO: 4204050.

However the complete sequence of the vector insert of Ghazal comprising SEQ ID NO: 4204050 was known in the prior art at the time the invention was made. Further, the parameters and objectives for generating probes were well known in the art at the time the invention was made. For example, Hogan taught methods for generating

target specific primers (col. 6-7, lines 50-67, lines 1-12), and provides extensive guidance for the selection of primers and probes. Hogan taught that "while oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 15 and about 50 bases in length" (column 10, lines 13-15). Accordingly it would have been obvious to one of ordinary skill in the art at the time of the invention to generate a probe of any length corresponding to any fragment of the CMV genome, including the portion identical to SEQ ID NO: 4204050 disclosed by Ghazal.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, James (Doug) Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of

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/Richard Schnizer, Ph. D./  
Primary Examiner, Art Unit 1635